



setting eggs on end resulted in the development of abnormalities. Hilaire thought that this was due to failure of formation of the air space whenever the large end of the egg was put downward. This finding was contrary to that of Réaumur, who stated that the air space always forms on the large end of the egg whether or not it is placed uppermost. St. Hilaire, the elder, also stated that malformations would be produced by tearing the embryo during early development, but Leuckart, who repeated some of Valentin's experiments confirming Hilaire, found that dividing the blastodisk did not give rise to malformation but stopped development. Although Gilis declared that St. Hilaire "penetrated the mechanism of the formation of monsters" showing that they are due to arrest of development through adhesions, Panum thought Hilaire's work too fragmentary to enable one to form any idea of its significance. According to Gilis, Swammerdam and Hilaire both tried to produce monsters experimentally, but only Hilaire succeeded. The younger Hilaire shook hen eggs horizontally before incubation and declared that such agitation prolonged the incubation period. He also removed part of the egg shell, coated the shells and pierced them with needles, but apparently without effect.

Panum, who made a very careful study of the occurrence of abnormalities in hen eggs before and during incubation, concluded that putrefying eggs are those that contain malformations. He undertook a carefully planned series of experiments to test this idea and to establish that malformations usually cause early death. According to Panum, "simple malformations" are more common in birds than in mammals, although he said that they were less common among birds than mammals among museum specimens. He found that eggs with a partly cracked shell would not develop if the crack was turned upward but that they would do so if it was turned downward, and declared that little was then (1860) known regarding the development of double eggs or of those with an "appendix."

It seems that Fremy and Valenciennes concluded that eggs with three or more yolks will not develop and that Jacobi (1765) stated that anomalies were more common in fish eggs which he attempted to fertilize artificially. Valenciennes found abnormalities more common in pike embryos which had been kept in too little water for seven hours, following artificial insemination. He found six such specimens in nine hundred and seventeen, all of them being accompanied by a single yolk.

Lereboullet (1852) also observed abnormal development in pike eggs which had been artificially inseminated, and all of which likewise were accompanied by a single yolk. Somewhat later he observed twenty-seven monstrosities in similarly inseminated fish eggs kept under unfavorable conditions. One of these had three heads and two trunks and hearts. Some of these instances of abnormal development were observed as early as

the time of formation of the "Nota primitiva" or notochord, and all were found on single yolks. Lereboullet never observed fusion of embryos which had developed on double yolks. It is interesting that Coste (1855) also observed abnormalities in artificially inseminated fish eggs having noticed a hundred in four thousand carp and salmon eggs.

Because Lihartzik (1858) had the idea that underdevelopment of the thorax was responsible for rickets and tuberculosis, he again investigated the effect of the position of the hen egg during incubation upon the course of development of the chick. He stated that when eggs were incubated with the large end uppermost, the head of the chick was smaller and the abdomen larger and the chick somewhat weaker, and declared that it remained so for some time after hatching. A reversal of the position of the egg was reported to have an opposite effect upon body form. When the egg was incubated in the horizontal position Lihartzik claimed that the pressure of the trunk against the head resulted in compression of the thorax, but nevertheless concluded from his experience with forty-eight eggs that the horizontal position is the most favorable one. Lihartzik's investigations confirmed those of Réaumur and contradicted those of St. Hilaire, who had stated that a horizontal position of the egg caused the development of abnormalities in the chick.

It is of special interest that a special commission was appointed in Denmark to determine the effect of irrespirable gases upon incubating eggs and that it found that development does not take place if the containers are tightly stoppered or sealed. Since it had been shown that development sometimes begins under warm water, it probably also did so in these cases unless the eggs were not incubated immediately after exposure to the gases.

Dareste (1856), who, according to Gilis, carried the art of producing monstrosities to a degree of perfection which was astonishing, found that varnishing the ends of eggs has a deleterious effect if done early in incubation, but not if it is done later on. He stated, that varnishing the large end resulted unfavorably in some cases because this treatment compelled the allantois to obtain relation with the shell in a nonvarnished area, and this he thought was the cause of the abnormalities. Dareste also varied the temperature during incubation and placed the eggs in various positions, as others had done before him. It seems that Dareste was the first to try the effect of electricity upon developing eggs and found that induction shocks produce malformations. He also showed that incubating the two halves of the hen egg at different temperatures results in unequal growth.

Panum, to whom I am mainly indebted for the above account, also mentioned the experiments of Poseleger, who coated eggs with oil, glue, and collodium, but found that none of these agents

affected the duration of the period of incubation, but that dipping eggs in wax prevented development altogether.

#### STUDIES ON FERTILIZATION OF THE OVUM

Soon after these earlier experimental investigations were made, embryology received more and more attention and much work was undertaken, especially upon the fertilization of the ovum. Some of these results were contrary to those obtained by earlier investigators with the hen egg. Morgan, for example, found that frog eggs when inverted gave rise to two embryos, and Hertwig found that amphibian eggs could be influenced to undergo meroblastic instead of holoblastic cleavage, and that keeping frog eggs in one to two per cent sodium chlorid solution retards development and frequently produces hemicrania and other developmental defects. Kolman by raising the temperature of eggs produced spina bifida, and others since then have produced a variety of abnormalities by changing the conditions of development such as the composition of the liquid or of the atmosphere in which the eggs were incubated, or by mechanical injury by puncturing, burning, and cutting or by rotation or exposure to radiations of various intensities and lengths. Anyone interested in the recent development of experimental embryology will find fascinating reading in Morgan's volume issued in 1927 and in a treatise on chemical embryology by Needham, published in 1931. For further information reference to the literature is indispensable.

Although Bonnet wrote to Spallanzani in 1781 saying that the mystery of fertilization was almost resolved, yet that mystery still faces us today. It is true that artificial insemination was done by the second Malpighi and that artificial fertilization was accomplished later on in some lower forms, but it should not be overlooked that even a full-grown "frog without a father," would not be the equivalent of one with a father. Although Boveri found that a portion of an ovum devoid of a nucleus can be fertilized by a spermatozoon and that development can thus be initiated and that separation of the first two blastomeres may result in the formation of an entire individual from each, these things are not possible in all

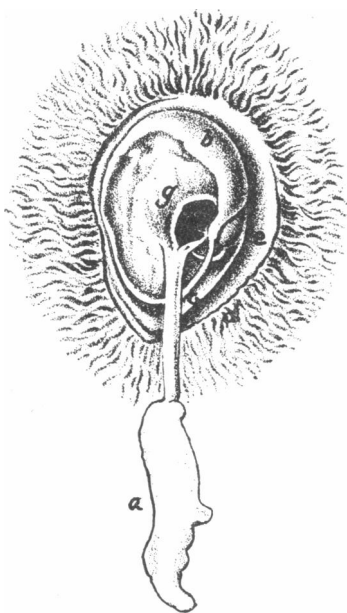


Fig. 7.—Human embryo with membranes, after von Baer, Table 4, Fig. 15. (a) embryo, (b) amnion, (c) serous lining, (d) chorion, (e) allantois, (g) insertion of umbilical cord. This is undoubtedly a retained macerated abortus (partly redrawn and relettered).

forms and can only be regarded as being highly suggestive indications for future work. It is highly improbable that it will be possible to substitute chemicals for the spermatozoon until the chemistry of the gene is fully understood, and that lies far in the future indeed.

As long as we shall remain ignorant of the true nature of the processes of development, we shall be compelled to add to the long list of words, "the mystical host," as Whitman called them, to designate hidden forces. In this list belong the first psychical causes or "psychic arche" or Aristotle; the archeus of Paracelsus; the impressio idealis of Harvey; the vis corporis essentialis of Wolff; the force expansiv or vis productrix of Needham; the nusus formativus of Blumenbach; the contactum vitalem, the virtute formatrix, and similar expressions of others. If such expressions as these are not used with an air of finality and are not permitted to become what Hertwig called "Ruhekissen," little harm is done. Even in the present day we speak of determinants and organizers. Although new terms are necessary to express a change in our point of view, all such expressions will possess only an historical interest in the near future.

Experimental embryologists working on lower vertebrates have done a very large amount of work since Roux began his important investigations on the mechanics of development and founded his well known Archiv. Many surprisingly interesting things have been revealed by this work, but no one can be at all certain as to how far the denouement peculiar to these very labile lower vertebrates typifies that in the higher. In the latter, experimentation is beset with much greater difficulties. It is natural that the chemical aspects of development are receiving an increasing amount of attention in these days of great interest in chemistry and that the physiology of reproduction also occupies an unusually prominent place in modern biological investigations. It is probable that a better understanding of abnormal development will come through experimental morphologic and chemical studies, although they can only be undertaken intelligently after the possession of detailed knowledge of normal development. This could only fail to be true if structure and function were not indissolubly joined; if not every functional change had a morphologic basis; if man could think without a brain.

#### STUDIES ON HEREDITY

One phase of embryology which has been developed so extensively by Morgan and his co-workers is of particular significance and importance to the physician. I refer, to be sure, to the work on heredity, regarding which even recent graduates in medicine are quite uninformed. This is highly regrettable and bound to entail personal and social disadvantages of a very serious kind. Although no one has yet seen a gene, anyone who stands in the rôle of personal or public advisor on health can no more act wisely without a knowledge of heredity than if he be ignorant of hormones or vitamins, yet this fact has received but slow recognition even in our medical schools.

## IN CONCLUSION

It has not been my aim to bring the history of embryology up to our day. So much has been accomplished in the last two generations that the review of this portion alone would be a considerable task and also one full of pitfalls. Although we know the history of the development of only a relatively few forms thoroughly, no one can encompass the entire field of embryology at present. Nor was it my aim to give the complete history of early embryology even. For that America lacks some of the indispensable literature.

I used the essay form because it permits greater freedom and have followed the chronological order in the main, but confined myself almost entirely to vertebrate embryology. I took little account of the philosophers and metaphysicians. There was enough speculation among naturalists, and the history of embryology shows that speculations regarding development approximated the truth inversely in proportion to their elaborateness. Observation and experiment always have accomplished more.

Imagination never has been able to fill gaps in our knowledge and has proven an unsafe guide. Narrowing the wide horizon of the unknown has been and can be accomplished only through observation and experiment. Although ultimate causes have eluded us, it often has been possible to learn something about how things happened even if not why they happened, and this probably will long remain true.

I have tried to convey something of the spirit of the older investigators by permitting them to speak for themselves. This could be accomplished only by quotations. Except for minor changes and some additions, these essays represent a series of lectures given for a half a decade, as an introduction to mammalian embryology. Many other topics could, hence, have been chosen and those considered could have been dealt with at greater length. I have deliberately avoided making a detailed analysis of the contribution of different investigators, for this could not be done without the introduction of many details of interest to the specialist only, and these essays are not intended for him.\*

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(The end)

\* Editor's Note: Complete list of references will appear in the reprints.

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*The First Appendectomy.*—Prof. Hermann Kümmell, surgeon of Hamburg, celebrated his eightieth birthday May 22. Kümmell was the first surgeon in Germany to perform the well known appendix operation (in 1889). He likewise pointed out ways for the elimination of cancer, for combating tuberculosis, and for the recognition of unobserved injuries of the spinal column. His researches have aided also in the spread of antisepsis and asepsis. He devoted himself primarily to surgery of the abdominal cavity and to disorders of the kidneys and of the urinary system. The handbook of surgery published by Kümmell in collaboration with Bier and Braun is known the world over.—*Journal of American Medical Association*, Vol. 99, No. 3.

## SOME MEDICAL EXPERIENCES IN PERSIA

BEING A COMPILATION OF LETTERS FROM THE  
LATE JOSEPH W. COOK, M. D.

LETTER II\*

A TRIP TO NEHAVEND IN LOORISTAN

Written at Hamadan, Persia,  
The American Hospital.

IT is interesting that in Persia every city or district is known for a certain characteristic. Isfahan, they say, is noted for the ability of its inhabitants to pull the wool over the eyes of prospective purchasers. Thus, Nehavend, where as I have said we went in May, is notorious for its miserliness. It is a city of some 16,000, of whom 1000 to 2000 are Jews. Nehavend is extremely rich in opium and tobacco, the opium in great demand for its high morphin content. But I never saw such terrible poverty; even the wealthy look poor and I saw no fine homes; the wealthy seem not to be willing to spend their money nor to know how to enjoy it. The city's curse is opium; 90 per cent of the population is addicted to it, they say, and without overstatement I fear; certainly the majority of my patients acknowledged their use of it. I did seven cataract operations, one iridectomy, fifteen hemorrhoid injections, twenty-five intravenous injections of typhoid vaccine for various conditions, fifteen neosalvarsan injections, two cauterizations for corneal ulcers, fifteen private calls, and saw 1933 patients during that week. It was very difficult to keep one's equilibrium. At 7 a. m. the sick would begin to come; scores of well-to-do were turned away for refusal to pay the examination fee; at the same time literally hundreds of poor people were seen and treated. Never have I seen such filth and such rags and such poverty, but behind them all I could see good faces and even some beauty. The women were interesting, rather longish faces, brown hair, gray-blue eyes, good features. But about 80 per cent had bad eyes, mostly trachoma so bad as to require weeks of persistent treatment to effect any sort of improvement. Fully 60 per cent had malaria or its effect; very few had anything that I could really help, but oh, the frantic passion to be examined and, as they hoped, cured! The crowd milled around the door, actually fighting for a chance to come in. It was hard, in such confusion, to make proper examinations. Suppose you had several children with chills and fever, or very bad eyes, no money to buy medicines even if you knew what to use; or suppose you had lost eight or ten children unborn and knew you would be thrust out by your husband, or perhaps had never had a baby and had already been thrown out by several husbands; or your husband was sick, even dying, and no one able to help; or you as a father were sick, unable to work, and four or five children starving?

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\* Letter I of this paper was printed in the September issue of California and Western Medicine, page 187.